Application No.: 10/573,130

Reply to Office Action dated December 12, 2007

## AMENDMENTS TO THE CLAIMS

Docket No.: 13111-00035-US

## **Listing of Claims:**

1. (Withdrawn) A process for preparing 3-methylamino-1-(thien-2-yl)propan-1-ol of formula I

comprising

- a) reacting thiophene with a  $\beta$ -halopropionyl halide or an acryloyl halide in the presence of a Lewis acid to give a 3-halo-1-(thien-2-yl)propan-1-one, with a hydrogen halide being passed in simultaneously or after the reaction has taken place, but before the reaction product is isolated, and
- b) reducing the propanone obtained in step a) and then, where appropriate without isolating the reaction product, reacting with methylamine.
- 2. (Withdrawn) The process as claimed in claim 1, wherein the Lewis acid used in step a) is aluminum trichloride.
- 3. (Withdrawn) The process as claimed in claim 1, wherein the reaction in step a) is carried out in a halogenated hydrocarbon as a solvent.
- 4. (Withdrawn) The process as claimed in claim 1, wherein the reduction in step b) is carried out using a metal hydride or semimetal hydride or using hydrogen in the presence of a transition metal catalyst as a reducing agent.
- 5. (Withdrawn) The process as claimed in claim 1 for preparing (S)-3-methylamino-1-(thien-2-yl)propan-1-ol of formula 1-S

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where appropriate in a mixture together with its R enantiomer I-R, with the propanol of formula I-S predominating in the mixture, wherein step b) is carried out in the presence of a chiral reducing agent or a chiral catalyst which exhibit selectivity with regard to the formation of (S)-3-methylamino-1-(thien-2-yl)propan-1-ol.

- 6. (Withdrawn) The process as claimed in claim 5, wherein a reducing agent is used in step b) comprising an asymmetric metal hydride or semimetal hydride or hydrogen in the presence of an asymmetric transition metal catalyst or wherein the reduction is carried out in the presence of a compound which mediates asymmetric induction.
- 7. (Cancelled).
- 8. (Currently amended) The process as claimed in claim [[7]] <u>27</u>, wherein the dehydrogenase is an alcohol dehydrogenase (E.C.1.1.1.1 or E.C.1.1.1.2).
- 9. (Currently amended) The process as claimed in claim [[7]] 27, wherein the dehydrogenase is selected from among dehydrogenases from yeasts of the genus Geotrichum, Pichia, Candida, Hansenula or Saccharomyces and from bacteria of the genus Pseudomonas, Burkholderia, Agrobacterium, Rhodococcus or Lactobacillus.
- 10. (Original) A process as claimed in claim 9, wherein the dehydrogenase is selected from among dehydrogenases from Geotrichum candidum, Candida magnoliae and Lactobacillus brevis.
- 11. (Withdrawn) An alcohol dehydrogenase having an amino acid sequence which, in the region of the N terminus

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a) comprises a constituent amino acid sequence of at least 10 consecutive *amino* acid residues as depicted in SEQ ID NO: 1, with the position corresponding to amino acid position 12 as depicted in SEQ ID NO: 1 additionally standing for valine; or a

- b) constituent amino acid sequence of at least 10 consecutive *amino acid residues* as depicted in SEQ ID NO: 2.
- 12. (Withdrawn) The alcohol dehydrogenase as claimed in claim 11 which is capable of reducing 3-chloro-1-(thien-2-yl)propan-1-one to (S)-3-chloro-1-(thien-2-yl)propan-1-ol.
- 13. (Withdrawn) The alcohol dehydrogenase as claimed in claim 12 which catalyzes the reduction in an enantiomeric purity of at least 85% ee (in the presence of NADH and/or NADPH; at 30°C and pH 6.0).
- 14. (Withdrawn) The alcohol dehydrogenase as claimed in claim 11 which is encoded by a nucleic acid sequence comprising SEQ ID NO: 3 or which comprises an amino acid sequence as depicted in SEQ ID NO: 4 or at least a constituent sequence as depicted in Figure 3, and can preferably be obtained from Lactobacillus brevis; and functionally equivalent alcohol dehydrogenases which are derived therefrom.
- 15. (Withdrawn) The alcohol dehydrogenase as claimed in claim 11 which is encoded by a nucleic acid sequence comprising SEQ ID NO: 5 or which possesses an amino acid sequence comprising SEQ ID NO: 6 and can preferably be obtained from Candida magnoliae (ATCC 12573); and functionally equivalent alcohol dehydrogenases which are derived therefrom.
- 16. (Withdrawn) A nucleic acid sequence which comprises a coding sequence for the dehydrogenase as claimed in claim 11, depicted in SEQ ID NO: 3 and 5; and derivatives which are derived therefrom.
- 17. (Withdrawn) An expression cassette which comprises a nucleic acid sequence as claimed in claim 15 in operative linkage with at least one regulatory nucleic acid sequence.

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18. (Withdrawn) A recombinant vector which comprises at least one expression cassette as claimed in claim 16.

- 19. (Withdrawn) A prokaryotic or eukaryotic host which is transformed with at least one vector as claimed in claim 17.
- 20. (Withdrawn) A method for preparing (S)-3-halo-1-(thien-2-yl)propan-1-ol comprising using the dehydrogenase as claimed in claim 11, or a natural or recombinant microorganism which produces this dehydrogenase.
- 21. (Currently amended) The process as claimed in claim [[7]] 27, wherein the dehydrogenase employed is an alcohol dehydrogenase having an amino acid sequence which, in the region of the N terminus
  - a) comprises a constituent amino acid sequence of at least 10 consecutive *amino* acid residues as depicted in SEQ ID NO: 1, with the position corresponding to amino acid position 12 as depicted in SEQ ID NO: 1 additionally standing for valine; or a
  - b) constituent amino acid sequence of at least 10 consecutive *amino acid residues* as depicted in SEQ ID NO: 2

or a dehydrogenase produced by a natural or recombinant microorganism.

- 22. (Currently amended) A process for preparing (S)-3-methylamino-1-(thien-2-yl)propan-1-ol of the formula I-S <u>comprising in-which reducing</u> a 3-halo-1-(thien-2-yl)propan-1-one is reduced enantioselectively, wherein the reduction is effected in the presence of a dehydrogenase, <u>producing a (S)-3-methylamino-1-(thien-2-yl)propan-1-ol of formula I-S</u>.
- 23. (Previously presented) The process as claimed in claim 21, wherein the (S)-3-halo-1-(thien-2-yl)propan-1-ol which is obtained in the reduction is reacted with methylamine without being isolated.

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24. (Previously presented) The process as claimed in claim 21, wherein the dehydrogenase is selected from among dehydrogenases from yeasts of the genus Geotrichum, Pichia, Candida, Hansenula or Saccharomyces and from bacteria of the genus Pseudomonas, Burkholderia, Agrobacterium, Rhodococcus or Lactobacillus.

- 25. (Previously presented) The process as claimed in claim 23, wherein the dehydrogenase is selected from among dehydrogenases from Geotrichum candidum, Candida magnoliae or Lactobacillus brevis.
- 26. (Previously presented) The process as claimed in claim 21, wherein the dehydrogenase is selected from among alcohol dehydrogenases selected from the group consisting of
  - a) a dehydrogenase capable of reducing 3-chloro-1-(thien-2-yl)propan-1-one to (S)-3-chloro-1-(thien-2-yl)propan-1-ol;
  - b) a dehydrogenase which catalyzes the reduction in an enantiomeric purity of at least 85% ee (in the presence of NADH and/or NADPH; at 30°C and pH 6.0);
  - c) a dehydrogenase which is encoded by a nucleic acid sequence comprising SEQ ID NO: 3 or which comprises an amino acid sequence as depicted in SEQ ID NO: 4 or at least a constituent sequence as depicted in Figure 3, and can preferably be obtained from Lactobacillus brevis; or functionally an equivalent alcohol dehydrogenase which is derived therefrom; and
  - d) a dehydrogenase which is encoded by a nucleic acid sequence comprising SEQ ID NO: 5 or which possesses an amino acid sequence comprising SEQ ID NO: 6 and can preferably be obtained from Candida magnoliae (ATCC 12573); or a functionally equivalent alcohol dehydrogenase which is derived therefrom.
- 27. (New) A process for preparing (S)-3-methylamino-1-(thien-2-yl)propan-1-ol of formula I-S

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## comprising

a) reacting thiophene with a β-halopropionyl halide or an acryloyl halide in the presence of a Lewis acid to give a 3-halo-1-(thien-2-yl)propan-1-one, with a hydrogen halide being passed in simultaneously or after the reaction has taken place, but before the reaction product is isolated, and

b) reducing the propanone obtained in step a) and then reacting with methylamine; wherein step b) is carried out in the presence of a dehydrogenase which exhibits selectivity with regard to the formation of (S)-3-methylamino-1-(thien-2-yl)propan-1-ol.